CLAIMS

What is claimed:

1. An isolated Rac-GEF polypeptide or a biologically-active fragment thereof.
2. An isolated Rac-GEF, or a biologically-active fragment thereof, of claim 1, wherein said polypeptide has a guanine nucleotide exchange activity, a specific binding affinity for a guanine nucleotide depleted Rac, or a cellular oncogenic transforming activity.
3. An isolated Rac-GEF or a biologically-active fragment thereof of claim 1 which is of human.
4. An isolated Rac-GEF of claim 1 comprising amino acid 1 to amino acid 711, as set forth in Fig. 1 (SEQ. ID NO: 2).
5. An isolated biologically-active fragment of Rac-GEF of claim 4 which comprises amino acids 273-605.
6. An isolated Rac-GEF, or a biologically-active fragment thereof, of claim 1, which is substantially purified.
7. An isolated nucleic acid comprising a nucleotide sequence coding for a Rac-GEF polypeptide.
8. An isolated nucleic acid of claim 7, wherein said coded for polypeptide has a guanine nucleotide exchange activity, a specific binding affinity for a guanine nucleotide depleted Rac, or a cellular oncogenic transforming activity.
9. An isolated nucleic acid of claim 7 which is human.
10. An isolated nucleic acid of claim 7, wherein the nucleic acid sequence codes for amino acid 1 to amino acid 711, as set forth in Fig. 1 (SEQ. ID NO: 2).
11. An isolated nucleic acid of claim 7, wherein the nucleotide sequence is operably linked to an expression control sequence.

12. An isolated nucleic acid of claim 7, wherein the nucleic acid comprises a naturally-occurring nucleotide sequence.

13. An isolated nucleic acid of claim 7, wherein the nucleic acid codes for said polypeptide without interruption.

14. An isolated nucleic acid of claim 7, wherein the nucleic acid is DNA or RNA.

15. An isolated nucleic acid of claim 7, wherein the nucleic acid further comprises a detectable label.

16. An isolated nucleic acid of claim 7, except where one or more amino acid positions are substituted or deleted, or both, and the polypeptide coded for by the nucleic acid is biologically-active.

17. An isolated nucleic acid of claim 16, wherein the biological activity is a guanine nucleotide exchange activity, a specific binding affinity for a guanine nucleotide depleted G-protein, or a cellular oncogenic transforming activity.

18. An isolated nucleic acid of claim 16, wherein the one or more substituted amino acid positions are substituted by conservative amino acids.

19. An isolated nucleic acid of claim 16, wherein the one or more substituted amino acid positions is in the Dbl homology domain or the pleckstrin homology domain.

20. An isolated nucleic acid comprising a nucleotide sequence which hybridizes, or whose nucleic acid complement hybridizes, under stringent conditions to base pairs of nucleotide sequence 900-1482 as set forth in Fig. 1 (SEQ. ID NO: 1).

21. An isolated nucleic acid claim 20 comprising at least 95% nucleotide sequence identity to the nucleotide sequence set forth in claim 20.

22. An isolated nucleic acid of claim 20, wherein said nucleic acid codes for a polypeptide having a guanine nucleotide exchange activity, a

specific binding affinity for a guanine nucleotide depleted Rac, or a cellular oncogenic transforming activity.

23. An isolated nucleic acid comprising a nucleotide sequence which is unique to Rac-GEF.

24. An isolated nucleic acid comprising a nucleotide sequence which hybridizes, or whose nucleic acid complement hybridizes, under stringent conditions to the unique nucleotide sequence of claim 23.

25. An isolated nucleic acid of claim 24 which codes for a polypeptide having a guanine nucleotide exchange activity, a specific binding affinity for a guanine nucleotide depleted Rac, or a cellular oncogenic transforming activity.

26. A method of expressing in transformed host cells, a Rac-GEF polypeptide coded for by a nucleic acid, comprising culturing transformed host cells containing a nucleic acid according to claim 7 under conditions effective to express the polypeptide.

27. A method of expressing, in transformed host cells, a polypeptide coded for by a nucleic acid, comprising culturing transformed host cells containing a nucleic acid according to claim 20 under conditions effective to express the polypeptide.

28. A method of claim 26, further comprising isolating the polypeptide.

29. A method of claim 26, further comprising modulating expression of the polypeptide.

30. An isolated polypeptide produced by a method of claim 26.

31. An isolated polypeptide produced by a method of claim 27.

32. A transformed host cell containing a nucleic acid of claim 7.

33. A transformed host cell containing a nucleic acid of claim 20.

34. A vector comprising a nucleic acid of claim 7.

35. A vector comprising a nucleic acid of claim 20.

36. A method of modulating an activity of a Rac polypeptide comprising, administering an effective amount of a Rac-GEF polypeptide or a biologically-active fragment thereof, or an effective amount of a compound which modulates the activity of the Rac-GEF.

37. A method of claim 36, wherein the Rac-GEF, or biologically-active fragment thereof, comprises an amino acid sequence which has a specific binding activity for a guanine nucleotide depleted state of said Rac.

38. A method of modulating an activity of a Rac polypeptide comprising;

introducing a nucleic acid of claim 21 into said cell under conditions whereby said nucleic acid is expressed in an effective amount to modulate said activity of Rac in said cell.

39. A method of claim 38 wherein said nucleic acid oncogenically transforms said cell.

40. A method of isolating a molecule that binds to a guanine nucleotide-depleted state of a Rac polypeptide comprising;

contacting a Rac polypeptide with a medium comprising said molecule under conditions effective for said molecule to bind to said Rac polypeptide; and

separating said Rac polypeptide to which said molecule has bound from said medium.

41. A method of claim 40, wherein said molecule is Rac-GEF.

42. A method of claim 40, wherein said molecule has a molecular weight of about 82.5 kilodaltons.

43. A method of claim 40, further comprising separating said molecule from said Rac polypeptide.

44. A method of modulating an activity of a GTPase comprising, administering an effective amount of a guanine nucleotide exchange factor or a biologically-active fragment thereof, or an effective amount of a compound which modulates the activity of the guanine nucleotide exchange factor.

45. A method of claim 44, wherein the guanine nucleotide exchange factor, or biologically-active fragment thereof, comprises an amino acid sequence which has a specific binding activity for a guanine nucleotide depleted state of said GTPase.

46. A method of testing for an agent which modulates the guanine nucleotide exchange activity of a guanine nucleotide exchange factor comprising:

contacting a mixture of (a) a polypeptide comprising a guanine nucleotide exchange factor, or a biologically-active fragment thereof, and (b) a polypeptide comprising a GTPase, or a biologically-active fragment thereof, to which the exchange factor can bind, with an agent; and

assaying for the presence or amount of guanine nucleotide exchange activity in the presence or absence of a GEF enhancer.

47. A method of claim 46, wherein the GTPase is Rac.

48. A method of claim 47, wherein the guanine nucleotide exchange factor is Rac GEF and paid GEF enhancer is ascorbyl stearate.

49. An agent identified by the method of claim 48.

50. A method of testing for an agent which modulates the binding between a guanine nucleotide exchange factor and a GTPase comprising:

contacting a mixture of (a) a polypeptide comprising a guanine nucleotide exchange factor, or a biologically-active fragment thereof, and (b) a polypeptide comprising a GTPase, or a

biologically-active fragment thereof, to which the exchange factor can bind, with an agent; and

detecting the presence or amount of binding between the guanine nucleotide exchange factor polypeptide, or the biologically-active fragment thereof, and the GTPase.

51. A method of claim 50, wherein the GTPase is Rac.

52. A method of claim 50, wherein the guanine nucleotide exchange factor is Rac-GEF.

53. An isolated agent identified by the method of claim 50.

54. An isolated antibody which is specific for a Rac-GEF or a peptide comprising a sequence present therein.

55. An isolated antibody of claim 54, which binds to an amino acid sequence selected from the group consisting of

H_2NAFRELIAOLELDPKCOOH

H_2NYQERTYKLPFSSFLCOOH

H_2NPQRSQNKDRRKLGSRNRQCOOH

56. A method of increasing the guanine nucleotide exchange activity of a guanine nucleotide exchange factor, or a biologically-active fragment thereof, said factor capable of acting on a member of the Ras superfamily of GTPases, comprising the steps of:

contacting said guanine nucleotide exchange factor, or a biologically-active fragment thereof, with said member of the Ras superfamily of GTPases, or a biologically-active fragment thereof; and

assaying for guanine nucleotide exchange activity under appropriate conditions in the presence of a guanine nucleotide exchange factor enhancer.

57. A method as described in claim 56 wherein said member of the Ras superfamily of GTPases is Rac and said guanine nucleotide exchange factor is Tiam-1.

58. A method as described in claim 57 wherein said GEF enhancer is selected from the group consisting of ascorbyl stearate, ascorbyl palmitate, and phosphoinositol.

59. A method as described in claim 58 wherein said phosphoinositol is selected from the group consisting of PI3,4,5P_3, PI4,5P_2 and PI4P.

60. A method of assaying for a compound to treat disease resulting from increased guanine nucleotide exchange activity of a guanine nucleotide exchange factor, or a biologically-active fragment thereof, said factor acting on a member of the Ras superfamily of GTPases, comprising the steps of:

contacting said guanine nucleotide exchange factor, or a biologically-active fragment thereof, with said member of the Ras superfamily of GTPases, or a biologically-active fragment thereof;

assaying for guanine nucleotide exchange activity under appropriate conditions in the presence of a guanine nucleotide exchange factor enhancer, and in the presence and absence of said compound; and

determining if said compound decreases said guanine nucleotide exchange activity.

61. A method as described in claim 60 wherein said member of the Ras superfamily of GTPases is Rac.

62. A method as described in claim 61 wherein said guanine nucleotide exchange factor is Tiam-1.

63. A method as described in claim 62 wherein said GEF enhancer is selected from the group consisting of ascorbyl stearate, ascorbyl palmitate, and phosphoinositol.

64. A method as described in claim 63 wherein said phosphoinositol is selected from the group consisting of PI3,4,5P_3, PI4,5P_2 and PI4P.

65. Compounds of claim 60 that decrease said guanine nucleotide exchange activity.

66. Ligands that bind to the Src homology 3 domain on Rac-GEF.

67. Ligands that bind to the Src homology 3 domain on Rac-GEF identified by the methods of claims 46 or 50.